of the foregoing amendments and these remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, it is noted that a shortened statutory period of three (3) months was set in the June 18, 2002 Official Action. The initial due date for response, therefore, was September 18, 2002. A petition for a three (3) month extension of the response period is presented with this amendment and request for reconsideration, which is being filed within the three (3) month extension period.

It is also noted preliminarily that claims 1-24 and 38-41 have been withdrawn from consideration in this application in accordance with the requirement for restriction set forth in the January 25, 2002 Official Action herein. Applicant's election of the subject matter of claims 25-37 for prosecution in this application is without prejudice to his right to file one or more continuing applications, as provided in 35 U.S.C. §121, on the subject matter of the non-elected claims.

Turning to the substantive aspects of the June 18, 2002 Official Action, claim 33 stands rejected under 35 U.S.C. §112 as allegedly indefinite due to the recitation of a trademark/trade name therein, i.e. PCR. Claim 33 has been amended by replacing "PCR" with "polymaraze chain reaction". Thus, any indefiniteness that may have been engendered by the original wording of claim 33 has been eliminated.

Claims 25, 27-31, 34, 36 and 37 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by each of

Peterson et al. (Biochem., 8(7):2916-23(1969)), Reeck et al. (PNAS, 69:2317-21 (1972)) and Kothari et al. (J. Chromat., 73:449-62 (1972)).

Claims 25, 26 and 35 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by pages 1556-60 of the Sigma catalog.

Claims 25, 27-31, 34, 36 and 37 also stand rejected under 35 U.S.C. §102(e) (pre-AIPA) as allegedly anticipated by U.S. Patent No. 5,843,663 to Stanley et al.

Claims 25-31, 33 and 34-37 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Peterson et al., in view of Reeck et al., Kothari et al. and the Sigma catalog pages. In formulating this ground of rejection, the Examiner acknowledges that none of the literature references cited as evidence of obviousness discloses the biological buffer BIS TRIS, and that the Sigma catalog pages do not disclose the immobilization of BIS TRIS on a solid support. The Examiner nevertheless concludes that it would have been obvious to one of ordinary skill in the art to combine the teachings of Peterson et al. with Reeck et al., Kothari et al. and the Sigma catalog pages because each of the cited literature references discloses the use of the immobilized biological buffer TRIS, which purportedly provides positively ionizable groups for isolating nucleic acids. The Examiner relies particularly on the disclosures of Kothari et al. and Reeck et al. which allegedly provide evidence that would make it obvious to one of ordinary skill in the art that the BIS TRIS biological buffer disclosed

in the Sigma catalog pages would be ideally suited for isolation of nucleic acids when immobilized on a solid surface. According to the Examiner, such a substitution is suggested because the BIS TRIS buffer described in the Sigma catalog purportedly shares the weak ionization properties of the TRIS buffer. The Examiner further asserts that the cited references provide the requisite motivation and reasonable expectation of success required to establish *prima facie* obviousness.

Claims 25-37 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Peterson et al. in view of Reeck et al., Kothari et al. and the Sigma catalog pages, and further in view of U.S. Patent Nos. 5,874,221 to Tooley et al. (hereinafter "Tooley") and 5,916,746 to Cobbs et al. (hereinafter "Cobbs"). According to the Examiner, it would have been obvious to one of ordinary skill in the art to combine the teachings of Peterson et al., Reeck et al., Kothari et al. and the Sigma catalog pages with Tooley and Cobbs, in view of the disclosure in the cited patents of a ion-exchanger which is the form of a tube or well or pipette tip and which is used in a method of isolating nucleic acids and in a polymerase chain reaction method. Here again, the Examiner asserts that the cited references provide the requisite motivation and reasonable expectation of success so as to establish that the subject matter of claims 25-37 would have been *prima facie* obvious.

The aforementioned rejections constitute all of the grounds set forth in the June 18, 2002 Official Action for refusing allowance of this application.

In accordance with the present amendments, independent claim 25 has been amended by changing the preamble to further characterize the utility of the claimed solid phase product and to recite that the ionizable groups are immobilized on a solid support. This amendment serves to distinguish the claimed products from the Sigma catalogue pages cited by the Examiner, showing that tubs of biological buffers per se are known. It is respectfully submitted that this amendment makes claim 25 novel over the Sigma catalog pages, as there is nothing in the Sigma catalog pages which corresponds to the solid support called for in claim 25. Claim 25 has been further amended to recite that:

> the ionizable groups...are effective at a first pH at which the ionizable groups are positively charged to bind nucleic acid present in a sample and are effective to release the nucleic acid at a second, higher, pH at which the charge on the ionizable groups is negative, neutral or less positive, the ionizable groups being provided by a chemical species..."

This language is derived from claim 1, as originally filed, and distinguishes the use of charge switch materials for binding and releasing nucleic acid, in accordance with applicant's invention, from prior art such as ion exchange chromatography columns, where elution is achieved using counter-ions (e.g. salt) to block the interaction of the ion exchange material with bound species. Unlike the charge switch materials of this invention, the pKa of ion exchange columns is deliberately chosen so that the ion exchange material will not protonate and deprotonate except at extremes of pH, and the elution of target species is achieved by varying salt conditions in the elution buffer.

The preamble of claim 26 has been amended to recite that the plurality of positively charged groups of claim 25 are provided by the specified Markush group of biological buffers.

Claim 34 has been amended to specify that the ionizable groups are provided by biological buffers and to include the subject matter of claims 35-37. Accordingly, claims 35-37 have been canceled. The various rejections of claims 35-37 are rendered moot as a result of their cancellation.

A new independent claim 42 has been added, which tracks claim 25, but calls for a Markush group of biological buffers as providing the ionizable groups. New claim 43 specifies the preferred biological buffer, Bis-Tris.

New dependent claims 44 to 47 correspond essentially to original claims 27 to 30.

New dependent claims 48 to 52 are directed to preferred solid phases, in particular covering beads. See pages 11 and 12 of the present specification for support.

New claim 51 is an independent claim specifying that the ionizable groups are provided by Bis-Tris.

New dependent claims 52 to 55 essentially track original claims 27 to 30.

New dependent claims 56 to 58 correspond essentially to new claims 48 to 50.

New independent claim 59 specifies both that the ionizable groups are provided by Bis-Tris and that the solid phase comprises beads.

New dependent claims 60 to 63 essentially track original claims 27 to 30.

New dependent claims 64 and 65 set out preferred types of beads. See page 12 of the present specification for support.

New dependent claims 66 to 68 correspond essentially to new claims 48 to 50, but are dependent on claim 25.

The specification has been amended to rectify apparent typographical errors appearing in Example 1 at page 32.

No new matter has been introduced into this application by any of the amendments presented herewith. Entry of this amendment is, therefore, respectfully requested.

As previously noted, the §112, second paragraph rejection of claim 33 is believed to be overcome by the foregoing amendment of claim 33. Accordingly, the only matters remaining to be addressed are the various prior art rejections set forth in paragraphs 5-11 at pages 3-9 of the June 18, 2002 Official Action. These last-mentioned grounds of rejection are respectfully traversed.

A. The Prior Art Cited in Support of the §102(b) Rejections of Claims 25-31 and 34-37 Fails to Constitute Evidence of Lack of Novelty

Rejections under 35 U.S.C. §102 are proper only when the claimed subject matter is identically disclosed or described in the reference cited as evidence of lack of novelty. In re Arkley, 172 U.S.P.Q. 524 (C.C.P.A. 1972). Applying this rule of law to the present case, the §102(b) rejection of claims 25, 27-31, 34, 36 and 37 based on each of Peterson et al., Reeck et al.,

and Kothari et al. and the §102(b) rejection of claims 25, 26 and 35 based on the Sigma catalog pages are improper because the subject matter of those claims, as now amended, is nowhere identically disclosed or described in the cited references.

Claims 25 and 27-31, as amended, call for a solid phase product comprising a plurality of positively ionizable groups, provided by chemical species from the group of biological buffers, polyhydroxylated amines, histidine and polyhistidine, which are immobilized on a solid support and which are "effective at a first pH at which the ionizable groups are positively charged to bind nucleic acid present in a sample and are effective to release the nucleic acid at a second, higher, pH at which the charge on the ionizable groups is negative, neutral or less positive at said first pH."

The just-quoted characteristic of applicant's product is referred to in the specification as "charge switching" and is accomplished by the use of a solid phase comprising "charge switch material". See pages 4-5 of the present specification for a general discussion of such material.

A schematic illustration of the use of applicant's charge switch material for isolation of nucleic acids is attached as Exhibit A. As can be seen in Exhibit A, the charge switch material is positively charged initially with suitable pKa properties and is effective to bind negatively charged nucleic acid. In order to release the bound DNA, the pH is altered to impart a more neutral charge to the solid phase so that the

positive charge is effectively switched off, thus losing its attraction for the nucleic acid.

Each of Peterson et al, Reeck et al. and Kothari et al. disclose ion exchange chromatography techniques for the analysis of biological materials. More specifically, Peterson et al. describes the use of ECTHAM Cellulose for the isolation of ribosomes, which are ribonucleoprotein particles composed of 60-65% ribosome RNA and 35-40% protein. Reeck et al. reports on the fractionation of nucleoprotein species in sonicated chromatin using ECTHAM Cellulose, chromatin being deoxyribonucleoprotein originating in cell nuclei. Kothari et al. is concerned with RNA fractionation on modified celluloses, including ECTHAM Cellulose, among others. None of Peterson et al., Reeck et al. or Kothari et al. disclose the "charge switching" aspect of applicant's invention. There is nothing in Peterson et al. or Reeck et al. or Kothari et al. to indicate that ECHTAM Cellulose is effective at a first pH at which the ionizable groups are positively charged to bind nucleic acid present in a sample and to release the nucleic acid at a second, higher pH at which the charge of the ionizable groups is negative, neutral or less positive than at the first pH, as required in applicant's claims 25-31. On the contrary, in carrying out ion exchange chromatographic techniques, such as described in Peterson et al., Reeck et al. and Kothari et al., elution is achieved by means of counter ions (e.g. from a salt-containing elution buffer), which serve to block the interaction of the ion exchange material with bound species. Unlike the charge switch materials of this invention,

the lower pKa of ion exchange columns is deliberately chosen so that the ion exchange material will not protonate and deprotonate, except at extremes of pH, and the elution of target material is achieved by varying salt concentrations in the elution buffer.

A schematic illustration of ion exchange chromatography is attached as Exhibit B, which shows an example of anion exchange chromatography. In this technique, anions in a mobile liquid phase (represented by squares) exchange with the negatively charged nucleic acid previously bound to the solid, positively charged anion exchange material. As can be seen in Exhibit B, the anion exchange material retains the identical charge during binding and release of the nucleic acid.

In assessing the disclosures of Peterson et al., Reeck et al. and Kothari et al. as evidence of lack of novelty in this case, it is noteworthy that ECTHAM Cellulose is prepared by modifying cellulose powder using Tris buffer and epichlorohydrin. This is substantially different from the chemistry used to prepare applicant's solid phase products, as described at pages 17 and 18 of the present specification. It is believed that the chemical reactions involved in producing ECTHAM Cellulose do not yield a material having the charge switch characteristic of the solid phase product claimed by applicant herein.

There is certainly no appreciation in Peterson et al., Reeck et al. or Kothari et al. of any charge switch characteristic possessed by ECTHAM Cellulose. In Peterson et al., the starting buffer and elution buffer have essentially the

same pH. The use of such conditions would not give rise to a charge switch, even if ECTHAM Cellulose were capable of undergoing charge switching (which is not disclosed in Peterson et al.). The process for chromotin fractionation described in Reeck et al. is expressly referred to as ion exchange chromatography. Compare Exhibit B. Kothari et al. is cumulative to Peterson et al., insofar as concerns the use of ECTHAM Cellulose for effecting isolation of ribisomes, providing a summary of the Peterson et al. reference which is cited herein.

The Sigma catalog pages relied on in support of the §102(b) rejection of claims 25, 26 and 35 clearly fail to anticipate those claims, as presently amended. There is no description in the cited Sigma catalog pages of a biological buffer immobilized on a solid support as called for in claim 25 and the claims that depend from claim 25.

Turning attention to claim 34 in its presently amended form, claim 34 is clearly patentably distinguishable from each of Peterson et al., Reeck et al. and Kothari et al., as none of those references disclose a water soluble product comprising a plurality of positively ionizable groups, which are provided by a biological buffer and which are separately attached to a polymer and/or polymerized, optionally by means of cross-linking reagents. ECTHAM Cellulose simply does not satisfy the requirements of claim 34. The same is true of the cited pages of the Sigma catalog, which make no mention of biological buffers providing a plurality of positively ionizable groups that are attached to a polymer or else are polymerized.

Inasmuch as neither Peterson et al. nor Reeck et al. nor Kothari et al. nor the cited pages of the Sigma catalog describe all of the claim recitations of applicant's claims 25-31 and 34-37, the §102(b) rejections based thereon are untenable and should be withdrawn.

B. Stanley et al. Fails to Constitute Evidence of Lack of Novelty with Respect to the Subject Matter of Claims 25, 27-31 and 34

The Examiner relies on Stanley et al. for its purported disclosure of a method of extracting nucleic acid from a sample, in which positively ionizable polyhydroxylated anion groups, histidine and polyhistidine groups are employed. However, Stanley et al. is not at all concerned with nucleic acid extraction employing a charge switch material, but rather with sequence specific nucleic acid extraction, in which nucleic acid in a sample binds to the solid phase by a hybrization reaction. This is in distinct contrast to the present invention in which the solid phase product functions on the basis of non-sequence specific binding properties. Sequence specific nucleic acid binding has considerable disadvantages for general nucleic acid purification as compared to the charge switch materials and methods of this invention, which are broadly applicable, have the capacity to be readily automated and can be incorporated easily into apparatus in common use in the laboratory such as beads, PCR tubes, pipette tips and the like.

The sequence specific nature of the binding employed in Staley et al. is evident from Column 1, lines 49-52, which

discloses that the nucleic acid analogs of the invention are "capable of hybridization to a nucleic acid of complimentary sequence". It is further disclosed in this connection, at Column 2, lines 1-6 of Stanley et al. that: "the nucleic acid analog is preferably capable of hybridizing to a nucleic acid of complimentary sequence to form a hybrid which is more stable against denaturation by heat than a hybrid between the conventional deoxyribonucleotide corresponding in sequence to said analog and said nucleic acid." The nucleic acid analogs disclosed in Stanley et al. are terminated with a chelating moiety capable of binding to a metal ion. The concept underlying the invention of Stanley et al. appears to be that the nucleic acid analogs hybridize to a target nucleic acid sequence in solution via sequence specific binding and are then bound to solid phases derivatized with metal ions as described, for example, at Column 5, lines 52-55.

Insofar as Stanley et al. mentions the use of histidine or polyhistidine, these function solely as chelating agents, for the purpose of binding to the metal ion-derivatize solid phase, and not as providing positively charged groups for binding to nucleic acid.

Claims 25, 27-31 and 34, as presently amended, are clearly distinguishable from Stanley et al. Regarding claim 25, the present amendment calls for positively charged groups provided by the charge switch material which are effective to bind nucleic acid at a first pH and release it at a second, relatively higher pH. As noted above, the nucleic acid analogs

of Stanley et al. do not function in this way. The histidine and polyhistidine disclosed in Stanley et al. as chelating agents are not intended to bind nucleic acid, and if they did so, such an interaction would prevent or hinder their functioning to bind the metal derivatized solid phase.

As for claim 34, this claim recites that the positively ionizable groups are provided by a group of biological buffers which do not include any of the materials disclosed in Stanley et al.

Like the references cited in support of the §102(b) rejection discussed above, Stanley et al. fails to constitute evidence of lack of novelty with respect to the subject matter of claim 25, 27-31 and 34. That being the case, the §102 rejection of those claims based on Stanley et al. is improper and should be withdrawn.

C. The Combined Disclosures of Peterson et al., Reeck et al., Kothari et al. and the Sigma Catalog Pages Fail to Render Obvious the Subject Matter of Claims 25-31 and 34-37, As Now Amended

All claim recitations must be considered in determining non-obviousness under 35 U.S.C. §103. In re Saether, 181 U.S.P.Q. 36 (C.C.P.A. 1974). It has long been held that when the Examiner disregards specific claim recitations that distinguish over the prior art, the rejection is improper and will be overturned. In re Glass, 176 U.S.P.Q. 489 (C.C.P.A. 1973). The three literature references cited in support of the §103(a) rejection of claims 25-31 and 34-37 clearly fail to suggest the

purification of nucleic acid using charge switch solid phases, in accordance with this invention. Rather, the purification methods disclosed in these references are either ion exchange chromatography methods or involve sequence specific binding, as discussed below.

Thus, Peterson et al. is largely concerned with ribosome isolation using chromatography, while Reeck et al. resolves components from chromatin (a protein DNA mixture), also via exchange chromatography. Kothari et al., as noted above, merely provides a summary of Peterson et al., insofar as it relates to ECTHAM Cellulose.

The inapplicability of ECTHAM Cellulose to nucleic acid purification is clearly connoted by the separate discussion in Kothari et al. of nucleic acid purification using derivatised celluloses on pages 455 et seq. The methods proposed in this section of Kothari et al. all involve the immobilisation of nucleotides or nucleic acid sequences so that the column binds sample nucleic acid <u>in a sequence specific manner</u>.

Applicants respectfully submit that it is rather misleading to say that the ECTHAM Cellulose disclosed in the cited literature references suggest applicants claimed charge switch approach to nucleic acid purification. At best, the references relate to ion exchange type purification of ribosomes or chromatin. The significance of this difference can be appreciated by referring to page 454, second paragraph of Kothari et al., which discloses that when ECTHAM Cellulose is being used as an anion-exchange material for ribosome purification, a salt

gradient is used to achieve fractionation of various components on the column, rather than using a change of pH to cause a charge switch material change its charge and release nucleic acid, as required in applicant's claims.

The development of means for efficiently and effectively isolating nucleic acid from a sample have been a goal long sought after in the field of molecular biology. If ECTHAM Cellulose were capable of achieving this goal, one would expect to find some indication of that in Peterson et al., Reeck et al. or Kothari et al.. When viewed objectively, however, the prior art disclosures of chromatographic isolation of ribosomes (Peterson et al. and Kothari et al.) and fractionation of chromatin (Reeck et al.), considered in conjunction with the Sigma catalog pages, in no way suggest the charge switch materials and methods of this invention. That being the case, the 35 U.S.C. §103(a) rejection of claims 25-31 and 34-37 based on the combined disclosures of Peterson et al., Reeck et al., Kothari et al. and the Sigma Catalog pages cannot be maintained.

D. The Combined Disclosures of Peterson et al., Reeck et al., Kothari et al., The Sigma Catalog Pages, Tooley and Grubbs Fail to Render Obvious the Subject Matter of Claims 25-37, as Now Amended

The basic deficiencies in the disclosures of Peterson et al., Reeck et al., Kothari et al. and the Sigma Catalog pages have been set out in detail above. The Examiner's additional reliance on Tooley and Cobbs clearly fails to compensate for those deficiencies.

The proposed combination of references cited in support of this rejection would scarcely have been made by the person of ordinary skill in the art without some motivation provided in the references themselves, which is plainly lacking.

It is quite evident, that Tooley and Grubbs, considered singly or together, have little, if any, relevance to the present invention. The disclosure of Tooley referred to by the Examiner describes the use of QIAGEN-tips to purify nucleic acid, which is then used directly for PCR after elution. A Qiagen tip contains a DEAE anion exchanger requiring high salt to elute the DNA followed by alcohol precipitation to recover the final product from the high salt solution. Importantly, the tips described in Tooley do not have charge switching properties, as required by applicant's claims. Furthermore, in Tooley there is no suggestion of carrying out the nucleic acid extraction using immobilised or polymerised biological buffer ions.

Grubbs has been cited because it lists certain solid phases (see column 6) used in nucleic acid purification, where the binding agent is attached to these phases. However, as can be seen from claim 1 (see column 10, lines 2-6), where the solid phases of '746 are used to bind target nucleic acid in a sample, they employ a polynucleotide probe. In other words, this is another example of a sequence specific hybridization method. Thus, this is quite similar to the disclosure of Kothari et al. relating to nucleic acid purification and, as such, is quite different from the charge switch products used in accordance with the present invention.

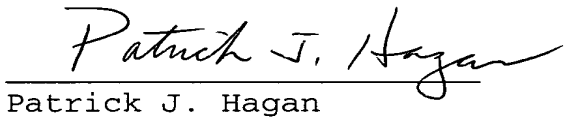
Even without his difference, it is noted that none of the materials disclosed in Grubbs appear to be biological buffers.

In summary §103(a) rejection of claims 25-37 based on the combined disclosures of Peterson et al., Reeck et al., Kothari et al., the Sigma Catalog pages, Tooley and Grubbs cannot properly be maintained in view of the present amendment to those claims and should, therefore, be withdrawn.

In view of the present amendments and foregoing remarks, it is respectfully requested that the rejections set forth in the June 18, 2002 Official Action be withdrawn and that this application be passed to issue, and such action is earnestly solicited.

DANN DORFMAN HERRELL and
SKILLMAN, P.C.

Attorneys for Applicant

By 

Patrick J. Hagan
Registration No. 27,643

PJH:ksk

Enclosures: Exhibits A and B

MARKED-UP VERSION OF REPLACEMENT PARAGRAPHS

A charge switchable ion-exchanger was prepared by covalently coupling polyhistidine to 100 [(m] μm glass beads using glutaldehyde by mixing 1 gram of the aminated glass beads with 0.01 %(v/v) glutaldehyde in 0.1M sodium bicarbonate at pH8 containing 20mg polyhistidine. After overnight incubation the beads were washed exhaustively to remove non-covalently bound material and stored in 10mM MES, pH5 containing 0.1 % (v/v) Tween 20.

About 300mg of the 100 [(m] μm derivitised glass beads were added to a 1ml plastic column enclosed at both ends.

A blood sample was incubated with an equal volume of 10mM MES pH5, containing 1% Tween 20, proteases (200 [(g] μg/ml) and 1 mM EDTA. After digestion is complete the blood was sucked up the column containing the glass beads and the DNA became immobilised allowing the contaminating proteins to pass through to waste.

Marked Up Copy of Amended Claims

25. (Amended) A solid phase product for use in a method [of extracting] in which the solid phase reversibly binds nucleic acid present in [from] a sample, the product comprising a plurality of positively ionizable groups, wherein the ionizable groups are immobilized on a solid support and are effective at a first pH at which the ionizable groups are positively charged to bind nucleic acid present in a sample and are effective to release the nucleic acid at a second, higher, pH at which the charge on the ionizable groups is negative, neutral or less positive, the ionizable groups being provided by a chemical species selected from the [list] group consisting of biological buffers, polyhydroxylated amines, histidine and polyhistidine.

26. (Amended) A product according to claim 25, wherein the plurality of positively charged groups are provided by a biological buffer which is selected from the group consisting of:

N-2-acetamido-2-aminoethanesulfonic acid (ACES);

N-2-acetamido-2-iminodiacetic acid (ADA);

amino methyl propanediol (AMP);

3-1,1-dimethyl-2-hydroxyethylamino-2-hydroxy propanesulfonic acid (AMPSO);

N,N-bis2-hydroxyethyl-2-aminoethanesulfonic acid (BES);

N,N-bis-2-hydroxyethylglycine (BICINE);

bis-2-hydroxyethyliminotrishydroxymethylmethane (Bis-Tris);

1,3-bistrishydroxymethylmethylaminopropane (Bis-Tris Propane);

4-cyclohexylamino-1-butane sulfonic acid (CABS);

3-cyclohexylamino-1-propane sulfonic acid (CAPS);

3-cyclohexylamino-2-hydroxy-1-propane sulfonic acid (CAPSO);

2-N-cyclohexylaminoethanesulfonic acid (CHES);

3-N,N-bis-2-hydroxyethylamino-2-hydroxypropanesulfonic acid (DIPSO);

-2-hydroxyethylpiperazine-N-3-propanesulfonic acid (EPPS);

-2-hydroxyethylpiperazine-N-4-butanesulfonic acid (HEPBS);

-2-hydroxyethylpiperazine-N-2-ethanesulfonic acid (HEPES);

-2-hydroxyethylpiperazine-N-2-propanesulfonic acid (HEPPSO);

2-N-morpholinoethanesulfonic acid (MES);

4-N-morpholinobutanesulfonic acid (MOBS);

3-N-morpholinopropanesulfonic acid (MOPS);

3-N-morpholino-2-hydroxypropanesulfonic acid (MOPSO);

piperazine-N-N-bis-2-ethanesulfonic acid (PIPES);

piperazine-N-N-bis-2-hydroxypropanesulfonic acid (POPSO);

N-trishydroxymethyl-methyl-4-aminobutanesulfonic acid (TABS);

N-trishydroxymethyl-methyl-3-aminopropanesulfonic acid (TAPS);

3-N-trishydroxymethyl-methylamino-2-hydroxypropanesulfonic acid (TAPSO);

N-trishydroxymethyl-methyl-2-aminoethanesulfonic acid (TES);

N-trishydroxymethylmethylglycine (TRICINE);

trishydroxymethylaminomethane (Tris);

polyhydroxylated imidazoles; and

triethanolamine dimers and polymers.

33. (Amended) A container according to claim 32 which is a [PCR] polymerase chain reaction or storage tube or well, or a pipette tip.

34. (Amended) A water soluble product for use in a method of extracting nucleic acid from a sample, the product comprising a plurality of positively ionizable groups, the ionizable groups being provided by a [chemical species selected from the list consisting of:]biological buffers; [polyhydroxylated amines; histidine; and polyhistidine;] wherein the plurality of ionizable groups are (i) separately attached to a polymer (ii) polymerised, optionally by means of cross-linking reagents or (iii) separately attached to a polymer and polymerized, optionally by means of cross-linking reagents; and wherein the biological buffer is selected from the group consisting of:

N-2-acetamido-2-aminoethanesulfonic acid (ACES);

N-2-acetamido-2-iminodiacetic acid (ADA);

amino methyl propanediol (AMP);

3-1,1-dimethyl-2-hydroxyethylamino-2-hydroxy propanesulfonic acid (AMPSO);

N,N-bis2-hydroxyethyl-2-aminoethanesulfonic acid (BES);

N,N-bis-2-hydroxyethylglycine (BICINE);

bis-2-hydroxyethyliminotrishydroxymethylmethane (Bis-Tris);

1,3-bistrishydroxymethylmethylaminopropane (Bis-Tris Propane);

4-cyclohexylamino-1-butane sulfonic acid (CABS);

3-cyclohexylamino-1-propane sulfonic acid (CAPS);

3-cyclohexylamino-2-hydroxy-1-propane sulfonic acid (CAPSO);

2-N-cyclohexylaminoethanesulfonic acid (CHES);

3-N,N-bis-2-hydroxyethylamino-2-hydroxypropanesulfonic acid (DIPSO);

-2-hydroxyethylpiperazine-N-3-propanesulfonic acid (EPPS);

-2-hydroxyethylpiperazine-N-4-butanesulfonic acid (HEPBS);

-2-hydroxyethylpiperazine-N-2-ethanesulfonic acid (HEPES);

-2-hydroxyethylpiperazine-N-2-propanesulfonic acid (HEPPSO);

2-N-morpholinoethanesulfonic acid (MES);

4-N-morpholinobutanesulfonic acid (MOBS);

3-N-morpholinopropanesulfonic acid (MOPS);

3-N-morpholino-2-hydroxypropanesulfonic acid (MOPSO);

piperazine-N-N-bis-2-ethanesulfonic acid (PIPES);

piperazine-N-N-bis-2-hydroxypropanesulfonic acid (POPSO);

N-trishydroxymethyl-methyl-4-aminobutanesulfonic acid (TABS);

N-trishydroxymethyl-methyl-3-aminopropanesulfonic acid (TAPS);

3-N-trishydroxymethyl-methylamino-2-hydroxypropanesulfonic acid (TAPSO);

N-trishydroxymethyl-methyl-2-aminoethanesulfonic acid (TES);

N-trishydroxymethylmethylglycine (TRICINE);

trishydroxymethylaminomethane (Tris);

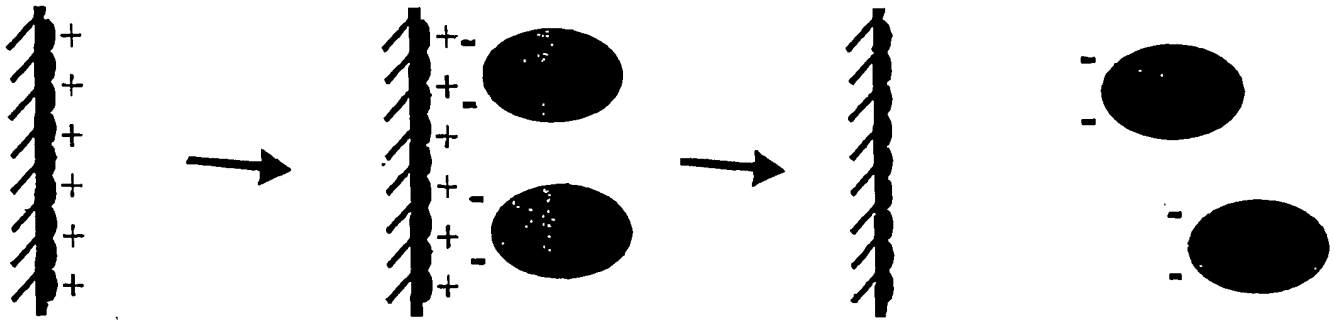
polyhydroxylated imidazoles; and

triethanolamine dimers and polymers.

EXHIBIT A

DNA Research Instruments

Charge Switch Technology



Positively charged solid phase with suitable pKa properties

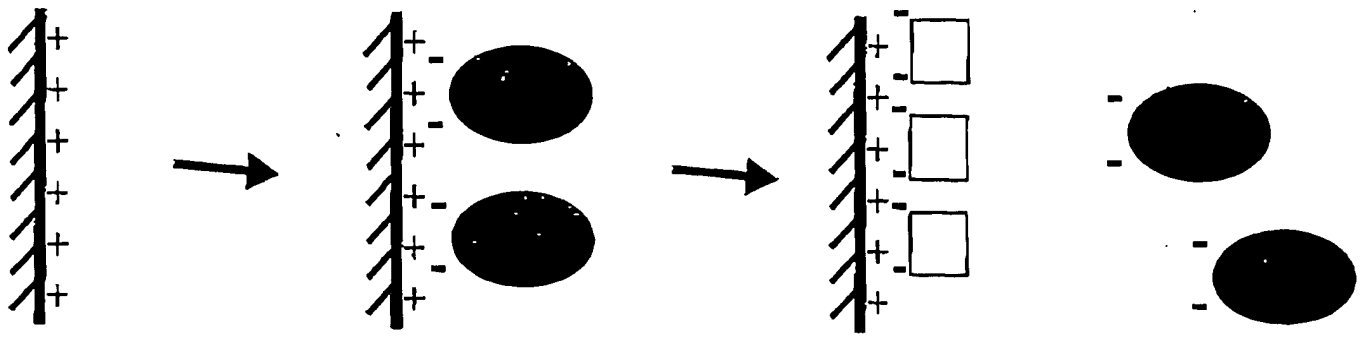
Negatively charged DNA binds to column due to charge

pH is altered so that the positive charge is effectively 'switched off' to allow the solid phase to have a more neutral charge and releasing the DNA

EXHIBIT B

DNA Research Instruments

Ion Exchange Chromatography



Positively charged ion exchange solid phase

Negatively charged DNA binds to column due to charge

DNA is displaced by high concentration of a negatively charged counter ion

August 29, 2002, are the most pertinent of which the undersigned is aware. However, no representation is made or intended that more pertinent references do not exist.

This submission is not an admission that the references listed on the attached Form PTO-1449 constitute prior art against the claims of this application.

The Examiner is respectfully requested to confirm receipt and consideration of the cited references by initialing and returning a copy of the attached Form PTO-1449 in accordance with MPEP §609.

Early and favorable consideration of this application is respectfully requested.

Respectfully submitted,

DANN, DORFMAN, HERRELL & SKILLMAN
A Professional Corporation
Attorneys for Applicant(s)

By Patrick J. Hagan

Patrick J. Hagan
PTO Registration No. 27,643

Telephone: (215) 563-4100
Facsimile: (215) 563-4044
Enclosures - Form PTO-1449
Copies of references listed on PTO - 1449